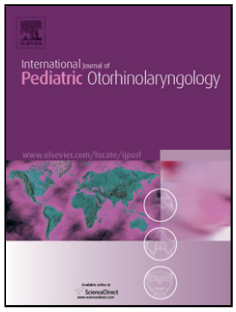

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Supraglottoplasty for Sleep Endoscopy Diagnosed Sleep Dependent Laryngomalacia

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ABSTRACT

Objective: To evaluate the polysomnographic outcomes of supraglottoplasty (SGP) performed for sleep endoscopy diagnosed sleep dependent laryngomalacia as treatment for obstructive sleep apnea syndrome (OSAS).

Methods: Nine subjects aged 6-55 months underwent supraglottoplasty for sleep dependent laryngomalacia. All subjects underwent both pre- and post-procedural polysomnograms.

Results: Supraglottoplasty for sleep dependent laryngomalacia resulted in improvement of OSAS as measured by collective improvements in 8 different primary polysomnogram parameters: apnea-hypopnea index (AHI), minimum (nadir) and mean oxygen saturation, mean and maximum carbon dioxide, total sleep time, sleep efficiency, arousal index, as well as improvement in weight for length percentiles. Subjects had a significant 80% decrease in percentage change in AHI ($P<0.005$), with decrease in mean AHI from 23.4 to 4.8 following supraglottoplasty. Seven of 9 subjects demonstrated improvement in nadir saturations, 6 of 9 subjects had improvement in sleep efficiency, and 7 of 8 subjects under 4 years of age had improvement in weight for length percentile.

Conclusion: Supraglottoplasty for sleep dependent laryngomalacia is an effective treatment of OSAS, and can be readily diagnosed using sleep endoscopy. Further investigation is warranted to increase awareness and outcomes related to sleep dependent laryngomalacia.

Keywords: sleep dependent laryngomalacia, supraglottoplasty, sleep endoscopy, obstructive sleep apnea syndrome, polysomnography, AHI

INTRODUCTION

Laryngomalacia, the prolapse of supraglottic structures into the glottic airway, is the most common laryngeal disease of infancy [1]. Laryngomalacia often presents as snoring, stridor, and difficulty feeding; in most cases the condition self-resolves as the child develops. Classically, the airway obstruction associated with laryngomalacia is less pronounced during sleep. However, some infants may develop sleep disturbance related to a certain variant of laryngomalacia [2-4]. This condition, termed sleep dependent laryngomalacia, is characterized by an increased work of breathing related to supraglottic collapse, most acute during sleep, and occasionally by its relatively late onset. The prevalence of sleep dependent laryngomalacia is currently unknown. Thus children with sleep dependent laryngomalacia often go on to have frank airway obstruction during sleep, consistent with Obstructive Sleep Apnea Syndrome (OSAS). OSAS in infants has been associated with failure to thrive, cognitive and behavioral deficits, and sudden infant death [1,5,6]. The etiology of laryngomalacia is typically determined via clinical history and exam, flexible fiber-optic laryngoscopy in clinic, or sleep endoscopy. The gold-standard diagnosis of OSAS is via overnight polysomnography (PSG) [1]. Surgical treatment of laryngomalacia is warranted only in severe cases (ie failed medical, dietary and behavioral modifications), and is indicated when symptoms include poor weight gain, episodes of respiratory distress, and OSAS [1]. Supraglottoplasty is the standard surgical intervention, and is defined as any procedure that modifies the supraglottis to alleviate the obstruction [1,7]. Supraglottoplasty in patients with sleep dependent laryngomalacia has been suggested to improve OSAS; however more investigations utilizing objective polysomnographic metrics are necessary to stratify and optimize patient outcomes [1,3,8,9]. The aim of this study was to review the impact of supraglottoplasty for children with sleep dependent laryngomalacia and OSAS, with the hypothesis that supraglottoplasty resulted in marked improvement in the severity of OSAS.

Methods

Subjects: Subjects from ages 6 to 55 months at the time of supraglottoplasty were identified retrospectively in one of two ways: by extraction from an institutional sleep endoscopy database from 2011-2013, or identified by Current Procedure Terminology coding (31540, 31541, and 31599). Of the subjects who had laryngomalacia diagnosed on direct airway visualization, those who subsequently underwent supraglottoplasty and who had both pre- and postoperative PSG were ultimately included in this review. Subjects' medical records were reviewed, and data from pertinent demographic, medical and operative histories, as well as PSG results, were entered into an Excel database. This study was approved by the institutional review board of Seattle Children's Hospital (SCH) (Seattle, Washington) and was conducted in compliance with the Healthcare Information Portability and Accountability Act.

Sleep Endoscopy and Supraglottoplasty: These procedures were done as part of routine clinical care. Sleep endoscopy was performed using a Pentax FNL-RP3 nasopharyngolaryngoscope under general anesthesia with "total intravenous anesthesia" technique. Patients were maintained in spontaneous ventilation in supine position on continuous propofol intravenous drip. Laryngomalacia was diagnosed if during inspiratory phase, supraglottic structures were noted to prolapse into the laryngeal introitus, obstruct respiratory flow and generate perturbation. Once diagnosed, all subjects underwent standard supraglottoplasty with division of aryepiglottic folds, redundant arytenoid mucosa reduction, and sparing of inter-arytenoid groove mucosa. Supraglottoplasty was performed using carbon dioxide laser, microdebrider, or micro-scissor technique by one of four fellowship trained pediatric otolaryngologists.

Polysomnography: PSGs were also obtained as part of routine clinical care, and performed at the American Academy of Sleep Medicine (AASM) accredited Pediatric Sleep Disorders Center at Seattle Children's Hospital. PSG data were collected on the Rembrandt ® (Buffalo, New York) or XLTEK ® (Oakville, Ontario, Canada)

systems. All studies were interpreted by board certified sleep physicians using AASM scoring criteria [10]. Both thermistors and nasal pressure transducers were used. End-tidal carbon dioxide was used interchangeably with transcutaneous carbon dioxide monitoring for the purpose of measuring ventilation. The AHI was calculated using the total number of obstructive apneas plus obstructive hypopneas per hour of sleep. The minimum oxygen saturation is reported as the oxygen nadir. The arousal index was defined as the number of 3-second cortical arousals per hour of sleep. For subjects who underwent split night titration studies, only the baseline diagnostic portions of the PSG are included in the results.

Data analysis: Analyses were largely descriptive, and correction for multiple comparisons was not done on this relatively small sample of retrospective data. Paired T-tests were used to compare preoperative and postoperative metrics within subjects, including AHI, nadir oxygen saturations, mean oxygen saturations, mean and maximum carbon dioxide, total sleep time, sleep efficiency, arousal index, and weight for length percentile. One sample T-tests were used to assess whether the percent change in each outcome metric was significantly different than the null hypothesis that there was no change between pre- and postoperative states. Significance was set using a two-tailed $p<0.05$. Logistic regression was run between continuous variables and correlations were examined to see if any preoperative characteristics were predictive of postoperative change. Statistical analyses were done on STATA 12 ® (College Station, TX).

Results

Initial search using CPT codes, as well as institutional sleep endoscopy database from 2011 – 2013, yielded 183 subjects. Of these 183 subjects who were between ages 6-55 months, 28 underwent supraglottoplasty, 18 of which were for sleep dependent laryngomalacia. Ultimately, nine subjects aged 6-55 months met the inclusion criteria of supraglottoplasty for sleep dependent laryngomalacia with pre- and postoperative polysomnograms; 7 of these subjects were diagnosed via flexible fiber-optic endoscopy. Two subjects were diagnosed via rigid telescope. Four out of 9 subjects underwent adenotonsillectomy immediately prior to supraglottoplasty.

Five of the 9 subjects were male and median age was 17 months (range, 6-55 months) at time of supraglottoplasty. Seven of 9 subjects (78%) had significant medical comorbidities, including agenesis corpus callosum (1), dysmyelination disorder (1), vocal cord paresis (1), and autism (1); 6 of 9 subjects were noted to have developmental delay, and 8 of the 9 subjects were documented to have some form of hypotonia. A summary of demographic and operative characteristics is provided in **Table 1**.

All children underwent PSG prior to supraglottoplasty, with the study occurring a mean of 91 days prior to surgery. All children also underwent polysomnography following surgery, with a mean of 155 days following the procedure. Collectively, all nine subjects had evidence of OSAS on preoperative study, as defined by an AHI of >1.5 [11]. If a more conservative definitions of OSAS is used of an AHI >5, then 8 out of 9 fell into this range.

As a group, subjects demonstrated improvement following PSG in each of the eight polysomnographic metrics: AHI, nadir saturation, mean oxygen saturation, mean and maximum carbon dioxide, total sleep time, sleep efficiency, and arousal index, though only comparison of AHI reached statistical significance on paired t-test. Subjects also improved comparing preoperative and postoperative weight to length percentiles. Subjects had a significant 80% decrease in percentage change in AHI ($P<0.005$), with decrease in mean AHI from 23.4 (range, 2.3-109.7) to 4.8 (range,

2.2-9.2), as demonstrated in **Figure 1**. Furthermore, 6 of 8 subjects transitioned from an elevated AHI into a commonly accepted "normal range" of AHI ≤ 5, with the ninth subject having no change (started and ended with an AHI <5). Other sleep metric improvements are outlined in **Table 2.** The 8 subjects under the age of 4 (cutoff age for CDC weight for length percentile) demonstrated a 115% improvement in weight for length percentile, with the percentile mean increasing from 34.4% (range, 0.6-93.3) before supraglottoplasty, and 74.2% (3.1-97.1) postoperatively. This is demonstrated in **Figure 3.** All three subjects with Failure to Thrive (as defined by the CDC as weight to length < 3rd percentile) improved to healthier levels above the 9th percentile. Improvement in nadir saturations is visually presented in **Figure 2.**

Preliminary correlations were examined between continuous variables to see if any preoperative characteristics were predictive of postoperative change. Regression analyses demonstrated a positive linear relationship between severity of preoperative AHI with post-operative improvement in AHI ($p<0.001$). The correlation can be examined in **Figure 4.**

Discussion

While the prolapse of epiglottic structures into the airway is oftentimes congenital and persistent during both periods of wake and sleep, it is of critical importance to acknowledge that many patients present with another form of laryngomalacia that is quite different. There are children with few or absolutely no breathing difficulties while awake, and then while sleeping parents note apnea, snoring, stridor, or other forms of noisy breathing. This may be present from birth, or acquired as the child develops. While the exact etiology of sleep dependent laryngomalacia is unknown, the best supported prevailing neurologic theory of laryngomalacia recognizes that the condition may be a result of an underdeveloped or abnormally integrated central nervous system, particularly the peripheral nerves and brainstem nuclei responsible for breathing and airway patency [12,13]. This discord is exacerbated

during periods of sleep, and offers an explanation for why work of breathing is most acute during sleep.

Despite the small size and retrospective nature of this study, this case series adds supportive data to a preliminary but growing literature linking sleep dependent laryngomalacia, OSAS as diagnosed with PSG, and supraglottoplasty as an effective treatment. Until recently, few studies have investigated the relationship between laryngomalacia and OSAS. Even fewer studies have explored the relatively new phenomenon of sleep dependent laryngomalacia. Smith et al [14] in 2005 and Richter et al [8] were amongst the earliest to demonstrate the efficacy of supraglottoplasty to alleviate sleep disordered breathing in children older than 12 months. However neither of these studies used polysomnographic metrics to objectively measure outcomes. More recently, Thevasagayam et al [15] diagnosed twelve children (median age, 5 years) with a form of late onset laryngomalacia, and 6 underwent supraglottoplasty. Only 3 of those 6 reported clinical improvement. In 2012 Digoy et al [2] demonstrated improvement in sleep dependent laryngomalacia after supraglottoplasty in 3 polysomnographic outcome fields; 39% of subjects were syndromic or had other comorbidities. In the same year Chan et al [3] demonstrated improvement in the AHI following supraglottoplasty for a form of late-onset laryngomalacia in 22 children (>2 years); 40% of these individuals had comorbid conditions and 13 of the 22 underwent an additional surgical intervention at time of supraglottoplasty. Thus, although the scientific community has commenced research examining the effect of supraglottoplasty on sleep dependent laryngomalacia, there is a compelling need to continue investigations.

In this study, 8 distinct polysomnographic metrics, both before and after supraglottoplasty, were utilized to demonstrate an improvement of OSAS in the setting of sleep induced laryngomalacia. Sleep disordered breathing, including OSAS, yields abnormal gas exchange in the patient, severely interfering with sleep's restorative processes and disrupting cellular and chemical homeostasis [16,17]. The resultant dysfunction of the prefrontal cortex has been shown to impair a child's attention, executive functioning, behavioral inhibition, self-regulation of affect and

arousal, and other socio-emotional behaviors [18]. More recent studies have investigated this in younger infants as well, suggesting that the presence of OSAS at a younger age may result in longer-term deficits well into childhood [5,16]. The significant decrease in AHI demonstrated in this study, along with improvement of other sleep parameters, decreases the risk these individuals will acquire considerable behavioral deficits in the future [4]. The correlation between preoperative AHI and postoperative improvement in AHI suggests that the higher the AHI was prior to supraglottoplasty, the larger the improvement in AHI postoperatively. This study is amongst the first to examine as many as 8 sleep parameters in sleep dependent laryngomalacia.

The above studies along with our presented data suggest that sleep dependent laryngomalacia is a significant and treatable disorder in some children. Sleep endoscopy is a novel diagnostic tool in the evaluation of children with obstructive sleep apnea which may lead to the observational diagnosis of sleep dependent laryngomalacia. At our center, this study has influenced decision making in that children who have unclear sources of obstruction with a history of stridor as an infant or while sleeping are more likely to be considered for sleep endoscopy. Some children who have no history of stridor may still be discovered to have sleep dependent laryngomalacia which presents a diagnostic challenge.

Limitations of this study are mostly inherent to a retrospective design. First, because these procedures and PSG were performed as part of clinical care, it is likely there is a referral bias, in that only those with the most pronounced clinical presentations underwent further testing. However, our results still add to the evidence base that supraglottoplasty can be incredibly beneficial and curative of OSAS. Given that other treatment options in this age group, such as positive airway pressure, are difficult to tolerate and tracheostomy is quite invasive, supraglottoplasty provides a relatively safe alternative. While many metrics examined demonstrate an improvement of OSAS, most did not reach statistical significance, likely due to limited sample size and the wide range of results that are not unexpected in a case series. While individuals with comorbidities fared well in

terms of AHI, it is possible that their medical conditions precluded improvement in other sleep parameters. It is important to consider clinical significance in this patient population, as all subjects saw an improvement on some parameters, and 7 of 8 charts from follow-up visits following supraglottoplasty explicitly reported better quality of sleep as perceived by caregivers, which is perhaps the strongest clinical indicator of success. Another limiting variable in the investigation is the novel interest in sleep dependent laryngomalacia. There is not a sole approach for managing patients with this phenomenon, and as a result the stratification and management of patients has yet to be streamlined, and is not identical. As a relatively new diagnosis, it certainly warrants further investigation.

Conclusion

When determining the origin of a child's OSAS, sleep dependent laryngomalacia is a diagnosis that may play a significant role in the condition, and warrants deliberate consideration. Sleep dependent laryngomalacia can safely and efficiently be diagnosed with sleep endoscopy. This investigation reports a series of 9 children for whom supraglottoplasty was shown to significantly reduce AHI, improving OSAS and thereby avoiding future growth and behavioral consequences.

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Table 1

Table 1	
Characteristic	**All Subjects**
Median age at time of surgery, m	17
Subjects, No.	9
Male:Female Ratio	5:4
Comorbid conditions, No. (%)	7 (78%)
Sleep Endoscopy performed at time of surgery No. (%)	7 (78%)
Days between pre-op polysomnography and SGP, mean	70
Days between post-op polysomnography and SGP, mean	184

Table 2

Polysomnography Comparison	Pre-supraglottoplasty Polysomnogram	Post-supraglottoplasty Polysomnogram	% Change	P-value
Total sleep time (min)	359.1	428.7	19.4	0.060
Sleep efficiency (%)	81.5	86.1	5.6	0.196
Apnea hypopnea index	23.5	4.8	-79.7	0.003
Mean SaO2 (%)	96.6	96.8	0.2	0.765
SaO2 nadir (%)	82.7	88.3	6.9	0.075
Mean ETCO2/TCOM (mmHg)	44.2	41.6	-6.0	0.266
Max ETCO2/TCOM (mmHg)	51.7	48.9	-5.5	0.393
Arousal index	17.7	12.4	-29.5	0.538
Weight:Length (%)	34.4	74.2	115.5	0.105

Legend to Tables and Figures

Table 1. Summary of patient demographic and operative characteristics.

Table 2. Polysomnographic measures before and after supraglottoplasty.

Figure 1. Effect of supraglottoplasty on Apnea Hypopnea Index.

Figure 2. Effect of supraglottoplasty on nadir SaO2.

Figure 3. Effect of supraglottoplasty on weight for length percentile.

Figure 4. Regression analysis of preoperative AHI with postoperative improvement in AHI.

Figure 1

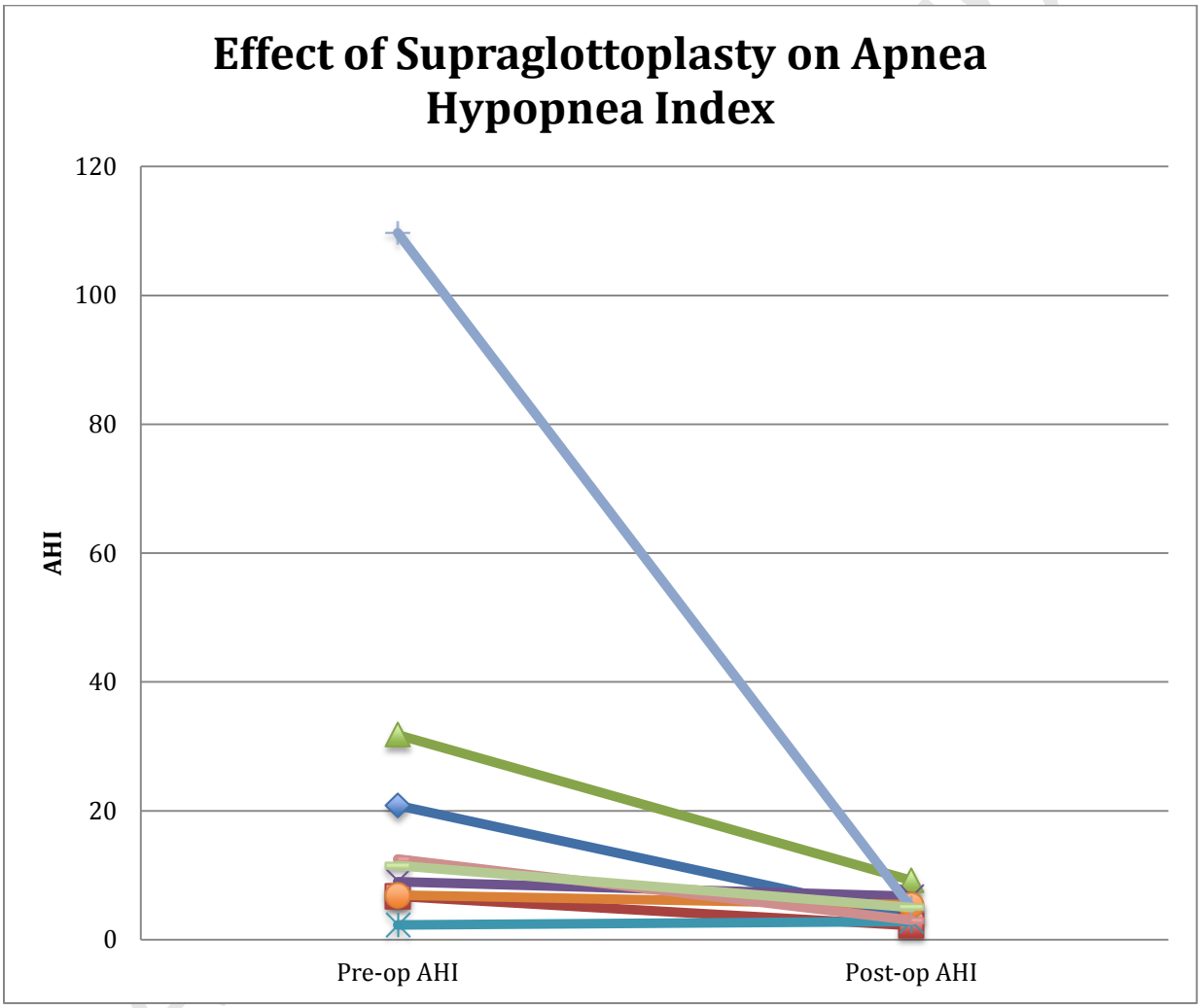

Figure 2

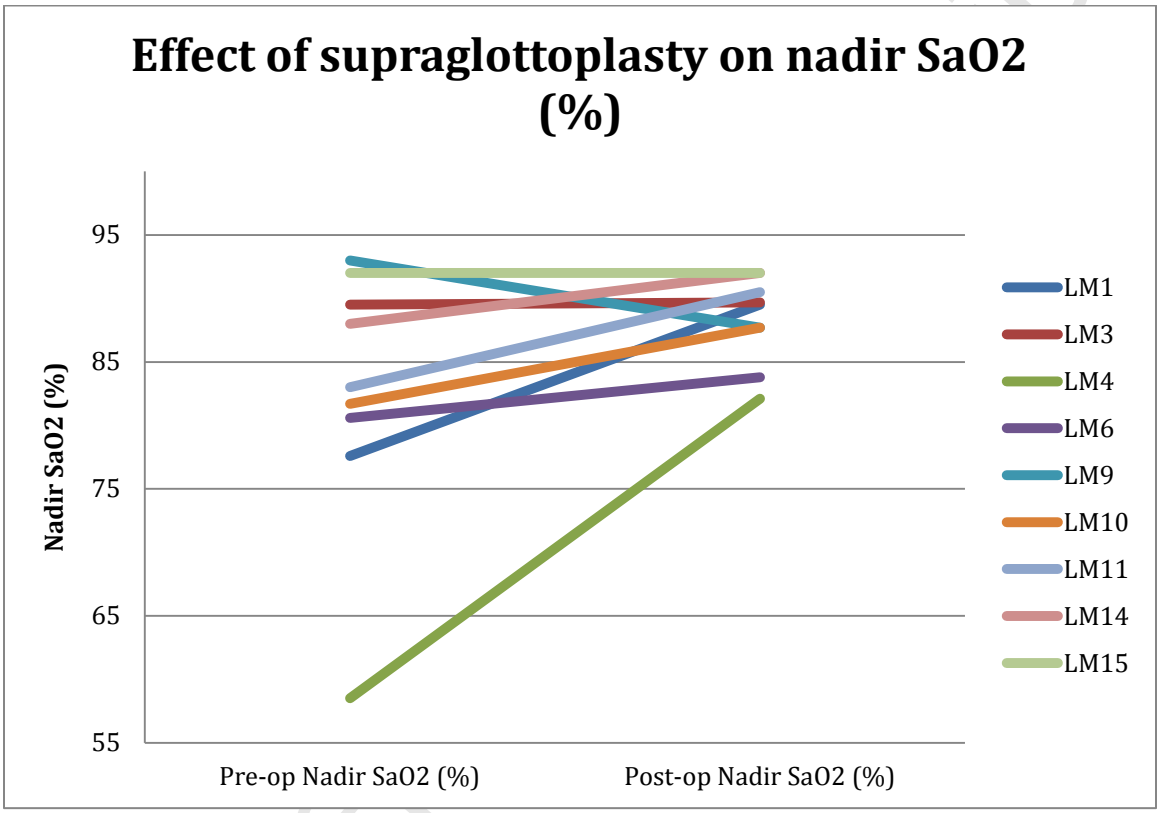

Figure 3

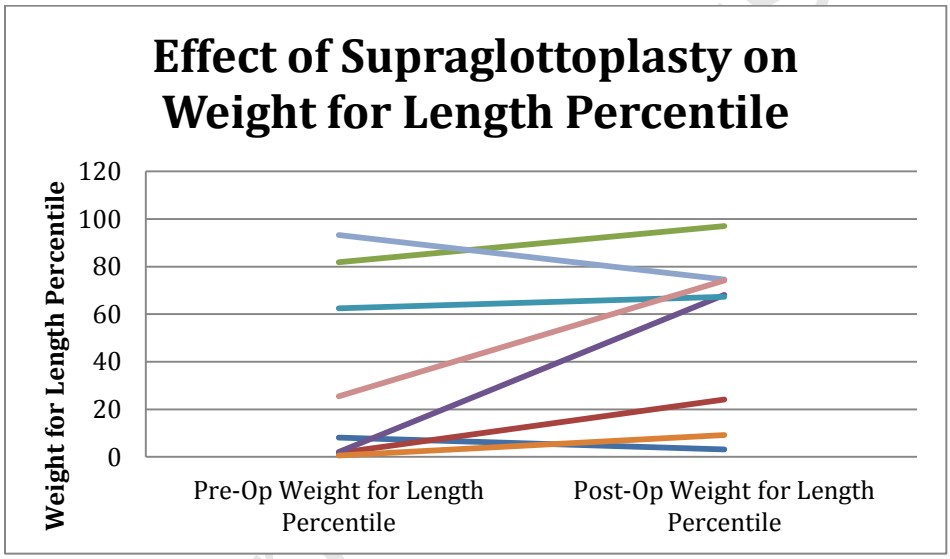

Figure 4